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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/004,230	10/31/2001	Lance E. Steward	17376	7851

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STEPHEN DONOVAN
ALLERGAN, INC.
T2-7H
2525 Dupont Drive
Irvine, CA 92612

EXAMINER	
NAVARRO, ALBERT MARK	
ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 04/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/004,230	STEWARD ET AL.	
	Examiner	Art Unit	
	Mark Navarro	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants amendment filed February 6, 2004 has been received and entered. Claims 9 and 11-14 have been canceled and new claim 10 has been added. Accordingly, claims 1-7 and 10 are pending in the instant application.

Claim Rejections - 35 USC § 112

1. The rejection of claims 1-7 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. Additionally this rejection is applied to newly added claim 10.

Applicants are asserting that the modified botulinum toxins of each pending claim have common distinguishing attributes. For example, independent claim 1 recites a modified botulinum toxin comprising at least one phosphorylation site as a secondary modification site. Further, the various phosphorylation sites that may be employed in accordance with claim 1 are identified, for example on Table 1 and 2 on pages 19-21 of the specification.

Applicants arguments have been fully considered but are not found to be fully persuasive.

Applicants arguments are not found to be fully persuasive in view of the Written Description guidelines, Federal Register, Vol. 64, No. 244, pages 71427-71440.

Applicants are asserting that the modified botulinum toxins of each pending claim have common distinguishing attributes. However, the claims recite a "modified botulinum toxin." This encompasses every single protein except a natural botulinum

toxin, since the degree of modification does not have an upper range limit and the claims do not set forth of any structural requirements that the modified toxin must retain. Furthermore, the claims recite "A modified botulinum toxin comprising at least one phosphorylation site added to the toxin..." The structure or identity of this phosphorylation site is not identified. The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, a "modified botulinum toxin comprising at least one phosphorylation site" alone is insufficient to describe the genus. Thus, Applicants have not described a function which is shared by the modified botulinum toxin which would adequately describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus.

For reasons of record in the previous Office Action, as well as the reasons set forth above, this rejection is maintained.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. The rejection of claims 4-5 rejected under 35 U.S.C. 102(b) as being anticipated by Johnson et al is maintained. Additionally this rejection is applied to newly added claim 10.

It is noted that this rejection is withdrawn from claims 1-3, and 6 in view of Applicants amendment.

Applicants are asserting that Johnson et al does not disclose a modified neurotoxin comprising a secondary modification site that may be the target of an enzyme for secondary modification, much less any particular secondary modification site such as phosphorylation site, glycosylation site, etc.

Applicants arguments have been fully considered but are not found to be fully persuasive.

Applicants assert that Johnson et al does not disclose a modified neurotoxin comprising a secondary modification site that may be the target of an enzyme for secondary modification, much less any particular secondary modification site such as phosphorylation site, glycosylation site, etc. However, Applicants are respectfully directed to the disclosure of Johnson et al, specifically claim 3. Claim 3 of Johnson et al discloses of a modified botulinum toxin in which a tyrosine residue is replaced by a threonine residue. Given that tyrosine is a phosphorylation site, and that this amino acid has been removed, the modified toxin disclosed by Johnson et al is "devoid of one or more secondary modification sites that are found in an identical naturally existing neurotoxin." Accordingly, Johnson et al disclose of each and every limitation set forth in the claims.

For reasons of record, as well as the reasons set forth above, this rejection is maintained.

3. The rejection of claims 1-7 rejected under 35 U.S.C. 102(b) as being anticipated by Montal et al is maintained.

Applicants are asserting that Montal et al do not teach of a secondary modification site. In other words, a phosphorylation itself is not a an amino acid sequence region "which may be targeted by an enzyme, for example an intracellular enzyme, to affect a modification to the site."

Applicants arguments have been fully considered but are not found to be fully persuasive.

Applicants assert that Montal et al do not teach of a secondary modification site. In other words, a phosphorylation itself is not a an amino acid sequence region "which may be targeted by an enzyme, for example an intracellular enzyme, to affect a modification to the site." However, Applicants are respectfully directed to the teachings of Montal et al. Montal et al specifically set forth of Clostridium tetani neurotoxins in which tyrosine residues have been modified to have a glutamate or aspartate residue in its place. (See abstract and claims). Those of ordinary skill in the art recognize that substitutions that result in changing serine, threonine, or tyrosine residues to charged amino acids such as glutamate or aspartate can result in an allele that mimics constitutive phosphorylation. (See for example, US Publication 2004/077039, summary). This is precisely what Montal et al has done, incorporated a glutamate or

aspartate residue in a neurotoxin sequence. The glutamate and aspartate residues are thus "phosphoryolation sites" added to the toxin, and are structurally different from a naturally occurring botulinum toxin. Again, each and every limitation has been addressed.

For reasons of record, as well as the reasons set forth above, this rejection is maintained.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro whose telephone number is (571) 272-

0861. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark Navarro
Primary Examiner
April 27, 2004